

**Clinical trial results:****TRATAMIENTO DE INDUCCIÓN CON RITUXIMAB + HYPER-CVAD Y ALTAS DOSIS DE METROTREXATO/CITARABINA Y CONSOLIDACIÓN CON Y90-IBRITUMOMAB TIUXETAN EN PACIENTES CON LINFOMA DE CELULAS DEL MANTO****Summary**

EudraCT number	2005-004400-37
Trial protocol	ES
Global end of trial date	09 September 2011

Results information

Result version number	v1 (current)
This version publication date	02 July 2021
First version publication date	02 July 2021

Trial information**Trial identification**

Sponsor protocol code	GELTAMO-LCM 04-02
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00505232
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GELTAMO
Sponsor organisation address	H. MARQUES DE VALDECILLA SERVICIO DE HEMATOLOGIA, SANTANDER, Spain, 39008
Public contact	GELTAMO, Grupo Español de Linfomas y Trasplante Autólogo de Médula Ósea (GELTAMO), 0034 913195780, dm@geltamo.com
Scientific contact	GELTAMO, Grupo Español de Linfomas y Trasplante Autólogo de Médula Ósea (GELTAMO), 0034 913195780, sc@geltamo.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 September 2011
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assessment of the safety profile of the treatment regimen

Protection of trial subjects:

Criteria for discontinuation of induction treatment

If levels are not recovered within 5 weeks to allow chemotherapy to be given

If grade 4 non-haematological toxicity, grade IV infection or severe bleeding (loss of 2 gr/dl of haemoglobin and life-threatening haemorrhage).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	30
Number of subjects completed	30

Period 1

Period 1 title	OVERALL TRIAL (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	LCM ARM
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	CICLOFOSFAMIDA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Intravenous use
Dosage and administration details:	
300 mg/m ² /12 hours iv, days 1, 2, 3	
Investigational medicinal product name	ADRIAMICINA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use
Dosage and administration details:	
25 mg/m ² iv, en infusión de 24 hours, days 4 y 5	
Investigational medicinal product name	VINCRISTINA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
1,4 mg/m ² iv (máximum 2 mg), infusion of 15', day 4 y 11	
Investigational medicinal product name	DEXAMETASONA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

40 mg/day, oral o iv, days 1 al 4 and 11 to 14

Investigational medicinal product name	RITUXIMAB
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m²

iv, day 1.

The first cycle could be administered without rituximab to avoid cytokine release syndrome.

Investigational medicinal product name	IBRITUMOMAB –TIUXETAN
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single dose of 0.3 mCi/Kg to be scaled up to 0.4

mCi/kg, according to study design. It is administered as a 10-minute i.v. infusion.

Number of subjects in period 1	LCM ARM
Started	30
Completed	30

Baseline characteristics

Reporting groups

Reporting group title	OVERALL TRIAL
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Reporting group description: -

Reporting group values	OVERALL TRIAL	Total	
Number of subjects	30	30	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	30	30	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	15	15	
Male	15	15	

Subject analysis sets

Subject analysis set title	All inclusion criteria
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Subject analysis set type	Full analysis
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Subject analysis set description:

Age between 18-70 years.

Diagnosis of mantle cell lymphoma (WHO classification 2008).

General condition 0 - 2 on the Zubrod scale.

Life expectancy greater than 3 months

Adequate bone marrow reserve, unless due to infiltration by lymphoma.

Hb 10 g/dL. PMN 1,500 cells/mm

3

platelets 100,000/mm³

Adequate hepatic, renal and cardiac function: creatinine <2.5x normal range, bilirubin or

ALT/AST < 2.5x LSN (upper limit of normal)

Cardiac LVEF > 50% (by echocardiography or perfusion scan).

Signed written informed consent of the subject or his/her legal representative.

Reporting group values	All inclusion criteria		
Number of subjects	30		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over	30		
Gender categorical Units: Subjects			
Female	15		
Male	15		

End points

End points reporting groups

Reporting group title	LCM ARM
Reporting group description:	-
Subject analysis set title	All inclusion criteria
Subject analysis set type	Full analysis
Subject analysis set description:	
Age between 18-70 years.	
Diagnosis of mantle cell lymphoma (WHO classification 2008).	
General condition 0 - 2 on the Zubrod scale.	
Life expectancy greater than 3 months	
Adequate bone marrow reserve, unless due to infiltration by lymphoma.	
Hb 10 g/dL. PMN 1,500 cells/mm	
3	
platelets 100,000/mm ³	
Adequate hepatic, renal and cardiac function: creatinine <2.5x normal range, bilirubin or	
ALT/AST < 2.5x LSN (upper limit of normal)	
Cardiac LVEF > 50% (by echocardiography or perfusion scan).	
Signed written informed consent of the subject or his/her legal representative.	

Primary: Primary

End point title	Primary
End point description:	
A response rate of more than 74% in patients treated with intensive first-line induction therapy (Rituximab + Hyper-CVAD and high-dose methotrexate/high-dose (Rituximab + Hyper-CVAD and high-dose methotrexate/cytarabine) 90-Ytrio-Ibritumomab at full dose	
cytarabine) 90-Ytrio-Ibritumomab full-dose	
End point type	Primary
End point timeframe:	
5 years	

End point values	LCM ARM	All inclusion criteria		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: >74%	30	30		

Statistical analyses

Statistical analysis title	Complete analysis
Statistical analysis description:	
The comparison will be made against a historical cohort on published data.	
Comparison groups	LCM ARM v All inclusion criteria

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
P-value	> 70
Method	Kaplan-Meier

Notes:

[1] - 70%

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the treatment

Assessment type	Non-systematic
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Dictionary used

Dictionary name	NCI-CTCAE
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Dictionary version	3.0
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Reporting groups

Reporting group title	All patients
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Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 30 (80.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm	Additional description: Second neoplasm		
subjects affected / exposed	4 / 30 (13.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	20 / 30 (66.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 30 (66.67%)		
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed occurrences (all)	19 / 30 (63.33%) 1		
Infections and infestations Mucositis management subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2007	see the induction treatment is modified so that the number of cycles will be 6, independent of age, rather than the 8 initially and not the 8 initially envisaged
29 October 2007	The obligation to pick up parents haematopoietic progenitors after the 5th cycle was withdrawn. Leaving collection to the discretion of the investigator

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported